First-in-Human Study of XMT-1536 in Cancers Likely to Express NaPi2b

Status: Recruiting

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

General Inclusion Criteria (for Dose Escalation, Expansion, and UPLIFT):

• ECOG performance status 0 or 1

• Measurable disease as per RECIST, version 1.1

• Resolution of all acute toxic effects of prior therapy or surgical procedures to ≤Grade 1 (except alopecia, stable immune-related toxicity such as hypothyroidism on hormone replacement, adrenal insufficiency on ≤10 mg daily prednisone [or equivalent], chronic Grade 2 peripheral sensory neuropathy after prior taxane therapy).

• Cardiac left ventricular ejection fraction (LVEF) ≥50% or ≥ the institution's lower limit of normal by either Echo or MUGA scan

• Adequate organ function as defined by the following criteria: 1. Absolute neutrophil count (ANC) ≥1500 cells/mm3 2. Platelet count ≥100,000/mm3 3. Hemoglobin ≥9 g/dL 4. In patients not on anticoagulation therapy: INR, activated partial thromboplastin time (aPTT), and prothrombin time (PT) all within 1.2 times the institution's upper limit of normal (ULN). Patients on anticoagulation therapy are allowed if their relevant laboratory values are within the therapeutic window. 5. Estimated glomerular filtration rate (GFR) ≥45 mL/min 6. Total bilirubin ≤ULN 7. g. Patients with asymptomatic elevations in unconjugated bilirubin due to Gilbert syndrome or stable chronic hemolytic anemia (e.g., hereditary spherocytosis, sickle cell disease, thalassemia intermedia) may be eligible after discussion with the Sponsor Medical Monitor.

• Aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT) ≤1.5 times the institutional ULN.

• Albumin ≥3.0 g/dL

• Able to provide informed consent. General Exclusion Criteria (for Dose Escalation, Expansion, and UPLIFT) :

• Major surgery within 28 days of starting study treatment, systemic anti-cancer therapy within the lesser of 28 days or 5 half-lives of the prior therapy before starting study treatment, or recent radiation therapy with unresolved toxicity or within a time window of potential toxicity.

• Patients with untreated CNS metastases (including new and progressive brain metastases), history of leptomeningeal metastasis or carcinomatous meningitis.

• Current known active infection with HIV, hepatitis B virus, or hepatitis C virus.

• Prior history of liver disease such as liver cirrhosis, hepatic fibrosis

• Current severe, uncontrolled systemic disease (e.g., clinically significant cardiovascular, pulmonary, or metabolic disease) or intercurrent illness that could interfere with per-protocol evaluations.

• Current use of either constant or intermittent supplementary oxygen therapy.

• History of suspected pneumonitis or interstitial lung disease.

• Pregnant or nursing women.

• History of other malignancy within the last 2 years, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or other malignancy with a similar expected curative outcome.

• Active corneal disease, or history of corneal disease within 12 months prior to enrollment

• Use of strong CYP450 3A inhibitors or inducers that cannot be discontinued while receiving study treatment

• Oxygen saturation on room air <93% Ovarian Cancer Inclusion Criteria for UPLIFT:

• Histological diagnosis of high grade serous ovarian cancer, which includes fallopian tube, or primary peritoneal cancer, that is metastatic or recurrent.

• Platinum-resistant disease 1. Patients who have only had 1 line of platinum-based therapy must have received at least 4 cycles of platinum, must have had a response [complete response/remission (CR) or partial response/remission (PR)], and then progressed between 3 months and ≤ 6 months after the date of the last dose of platinum 2. Patients who have received 2 to 4 lines of prior therapy must have received at least 4 cycles of platinum and then progressed within 6 months after the date o the last dose of platinum

• One to 4 prior lines of systemic therapy for ovarian cancer a. Prior treatment with bevacizumab is required for patients with 1 to 2 prior lines of therapy

• Patients must be willing to provide an archival tumor tissue block or slides or if not available, undergo procedure to obtain a new tumor biopsy using a low-risk, medically routine procedure Ovarian Cancer Exclusion Criteria for UPLIFT:

• Low-grade, clear cell, endometrioid, mucinous, carcinosarcoma, germ-cell, mixed histology, or stromal tumors

• Prior treatment with mirvetuximab soravtansine or another ADC containing an antitubulin payload

• Primary platinum-resistant disease, defined by a lack of response or by progression within 3 months after completing front-line, platinum-containing therapy.

• Participation in DES or EXP segments of this study Ovarian Cancer Inclusion Criteria for QTc sub-study: Note: patients must meet all UPLIFT cohort inclusion criteria in order to participate in the QTc sub-study • Study patient has agreed to remain in the clinic for the additional QTc related study activities on the Day 1 of Cycle 1 and Cycle 3. Ovarian Cancer Exclusion Criteria for QTc sub-study:

• Use of strong CYP450 3A inducers.

• Uncontrolled cardiac arrhythmias, for example, atrial fibrillation with a ventricular response at rest > 100 beats per minute. left bundle branch block (LBBB)

• Known abnormality of any cardiac valve (either stenosis or regurgitation) that is greater than moderate in severity.

• Subjects not in sinus rhythm at screening with HR >45- <100

• Any ECG abnormality that can interfere with the measurement of the QT interval

Conditions & Interventions

Interventions:

Drug: upifitamab rilsodotin

Conditions:

Platinum Resistant Ovarian Cancer, Non Small Cell Lung Cancer Metastatic

More Information

Contact(s): Jamie Barrett - medicalinformation@mersana.com

Principal Investigator: Randall, Leslie
Phase: Phase 1/Phase 2
IRB Number: HM20020050
System ID: NCT03319628
